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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,592	03/11/2004	Robert A. Herrmann	00-0193 D1	6360

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
08/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,592	HERRMANN ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *23-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' Terminal Disclaimer and amendment, both filed 05/01/2008.

Claims 1-39 are pending.

Claims 23-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 08/22/2007.

Claims 1-22 are included in the prosecution.

Terminal Disclaimer

1. The terminal disclaimer filed on 05/01/1008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 6,706,274 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The following rejection has been overcome by virtue of applicants' amendment and remarks:

The rejection of claims 1-22 under 35 U.S.C. 112, second paragraph, as being indefinite.

The following rejection has been discussed in details in the previous office action and is maintained for reasons of records:

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,287285 ('285) combined with the article "S-Nitrosothiols cause prolonged, nitric oxide mediated relaxation in human saphenous vein and internal mammary artery: therapeutic potential in bypass surgery" by Sogo et al.

US '285 teaches medical device inserted into the vasculature of patient such as cardiac leads comprising nitric oxide (NO) donating compounds incorporated in solution or polymer (abstract; col.2, lines 28-31; col.5, lines 8-15; col.19, claim 14). The NO compounds include one or more NO donor compounds selected from the group containing of S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione (col.20, claim 20). Therapeutic agents can be included in the device including amino acids (col.4, line30).

Although the reference suggested inclusion of more than one NO donor in the medical device and disclosed 7 preferred members of NO donors included S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione, however, the reference does not explicitly teach the combination of S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione.

Sogo et al. teach that S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione produce more relaxation of vessel walls than commonly used NO donors, and more specifically, teach that the relaxation caused by S-nitroso-N-acetyl-D,L-penicillamine was more sustained, and S-nitrosoglutathione selectively dilates human arteries in vitro and in vivo, and their use might improve the outcome of coronary artery bypass (page 1237, left col.; page 1241, right col.; page 1243, left col.).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide medical device for vascular use comprising more than one NO donor compounds as disclosed by US '285, and select S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione from the group of 7 NO donors disclosed by US '285, motivated by the teaching of Sogo et al. that these two NO donor compounds produce more relaxation of vessel walls than commonly used NO donors with prolonged sustained relaxation and dilatation of human arteries, and their use might improve the outcome of coronary artery bypass, with reasonable expectation of having medical device for vascular use comprising S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione that successfully provides prolonged sustained relaxation and dilatation of human arteries, with improvement on the outcome of coronary artery bypass.

The combination of the references teaches the same first nitric oxide donor and second nitric oxide donor as instantly claimed, therefore, the half-life, activity, release rates, and susceptibility to metal ion catalyst release are expected to be the same as those recited by the instant claims.

Response to Arguments

5. Applicant's arguments filed 05/01/2008 have been fully considered but they are not persuasive.

Applicants argue that Michal et al. (US '285) fails to teach a combination of two NO donor compounds in the medical device or to provide any explicit statement of using

a combination of NO donor compounds, and the only passage of Michal et al. that suggests such a combination is claim 20 of Michal et al., which claims: one or more nitrogen oxide donating compounds selected from the group consisting of2-methyl-2-aitrosopropane, S-Nitroso-N- acctyl-D,L-penicillamine, 3-morpholoinosydoimine, sodium nitrate, s-nitrosoglutatione, sodium nitroprusside, and nitroglycerine. Applicants argue that such a claim that lists multiple compounds as a potential therapeutic agent does not, teach or suggest a combination of two NO donor compounds to meet the obviousness standard that the prior art reference must teach or suggest all of the claimed features. Applicants further argue that Michal's reference fails to provide an enabling disclosure for the specific features of the claimed medical article.

In response to this argument, applicant's attention is directed to the scope of the present claims that are directed to product, and all the element claimed product are disclosed by the combination of the prior art. Michal's reference suggested combination of one or more nitric oxide donors selected from only six members, therefore, possibility to obtain the specific claimed combination is low. The combination of two or more nitric oxide donors is claimed by the reference, i.e. preferred embodiment. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to

one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

Applicants argue that secondary reference, Sogo et al. does not teach a combination of NO donor compounds. Sogo et al. presents nitrosoglutathione and N-(S-nitroso-N-acetylpenicillamine) as alternatives, rather than as a combination. Nowhere does Sogo et al. teach using both NO donors in conjunction with one another.

In response to this argument, it is argued that combination is already taught by Michal et al., and Sogo et al. is relied upon for teaching the species of each NO donor as being advantageous for treating vessel walls. Teaching the advantage of each of the NO donor would have motivated one having ordinary skill in the art to select these specific donors because Sogo et al. teaches that these two NO donor compounds produce more relaxation of vessel walls than commonly used NO donors with prolonged sustained relaxation and dilatation of human arteries, and their use might improve the outcome of coronary artery bypass.

Applicants argue that the examiner relies on inherency to remedy the deficiency of the combined references in teaching a combination of NO donor compounds. However, that which is inherent in the prior art, is not known as the same of the invention, cannot form a proper basis for rejecting the claimed invention as obvious under 35 U.S.C. §103. A holding of inherency must flow as a necessary conclusion from the prior art, not simply a possible one. Inherency may not be established by probabilities or possibilities.

In response to this argument, it is argued that compounds and their properties are inseparable, and if the combined prior art teaches the elementary compounds of the product of the claims, then the properties of the claimed product are the same as the prior art. It is further argued that the half-life of each compound is inherent, and if the combination of the prior art teaches the same claimed NO donors, then each of them has the same half-life period, wherein one is longer than the other. In any event, the discovery of a new action underlying a known material does not make it patentable. *MEHL/Biophile*, 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. Also, it is irrelevant that the prior art observers did not recognize the property or function of the disputed claim; if the prior art inherently possessed that characteristic, it anticipates. See *Verdeegal Brothers, Inc. v. Union Oil Co. of Cal.,* 814 F.2d 628, 633, 2 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 1987). This is believed to be applicable here because anticipation is the epitome of obviousness.

Applicants further argue that the addition of the disclosure of Sogo et al. to that of Michal et al. relies upon the use of undue hindsight, which is prohibited.

In response to this argument, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants argue that the teachings of the references are not properly combinable without motivation and suggestion to combine them found in the references themselves.

In response to this argument, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide medical device for vascular use comprising more than one NO donor compounds as disclosed by US '285, and select S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione from the group of 7 NO donors disclosed by US

'285, motivated by the teaching of Sogo et al. that these two NO donor compounds produce more relaxation of vessel walls than commonly used NO donors with prolonged sustained relaxation and dilatation of human arteries, and their use might improve the outcome of coronary artery bypass, with reasonable expectation of having medical device for vascular use comprising S-nitroso-N-acetyl-D,L-penicillamine and S-nitrosoglutathione that successfully provides prolonged sustained relaxation and dilatation of human arteries, with improvement on the outcome of coronary artery bypass. It has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int 'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.,* 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions."

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Isis A Ghali/
Primary Examiner, Art Unit 1611

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